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Statement of the Biotechnology Industry Organization
to the HHS Task Force on Drug Importation

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Natcher Auditorium, Building 45, National Institutes of Health (NIH)
9000 Rockville Pike, Bethesda, MD 20892

The Biotechnology Industry Organization (BIO) appreciates the opportunity to present its views on the issue of altering current standards and requirements to allow the legal importation into the United States of prescription drugs that currently cannot be imported legally, either because they are not FDA-approved or because the entities or individuals importing them are not permitted to do so under current law.

BIO represents more than 1,000 biotechnology companies, academic institutions, state biotechnology centers and related organizations in 45 U.S. states. BIO members are involved in the research and development of health-care, agricultural, industrial and environmental biotechnology products.

Many BIO members develop and manufacture life-saving prescription products that often are administered intravenously or by injection; many require both the intervention of and close supervision by a health care professional. Most of these biological and biotechnology products are solutions. Many are extremely sensitive to changes in manufacturing parameters, temperature, light, pressure, and shipping and handling conditions. In addition, because they often are clear liquids, it can be extremely difficult to detect when the products may have been opened and thus contaminated, diluted, or exposed to improper light or temperature conditions and thus rendered less effective or ineffective, or simply replaced in a vial by plain water. Indeed, all of these things have happened to biological products over the course of the last several months. Many of these incidents have been reported in the press and FDA has issued alerts to health care practitioners and patients.

Because of the sensitivity of biological and biotechnology products, congressional importation proposals generally have exempted many biological products, injectable and infused products, and others from provisions that would legalize the importation of prescription drugs. Such exemptions, however, do not set our minds at ease. One need only look at the astonishing numbers of prescription products entering the U.S. via mail and consignment carrier every day to know that illegality or exemptions are merely words on paper. For unscrupulous vendors and unwitting patients, the fact that it is illegal to import virtually all of these products and that importing some of them is especially dangerous seem to be no deterrent at all. That is why, notwithstanding the well-intentioned exemption of most of our member companies' products, BIO continues to oppose the legalization of expanded drug importation.

Background

BIO believes, and we think we share this view with most American patients, that the United States system of drug regulation is the world's gold standard. Our approval system assures patients that their medications have been shown to be safe and effective, our manufacturing requirements provide them assurance of product quality and consistency, and our distribution controls have provided great confidence in the integrity of the drug supply. In many other countries, there are no such guarantees and patients literally cannot know whether the prescriptions they receive are pure or adulterated, potent or ineffective, real or fake. That reality is one we have not had to face in America – until now. It was alarming to hear testimony last year from a senior Florida health official that the prescription drug supply in Florida had reached a point where patients filling prescriptions in legitimate, licensed pharmacies literally did not know where the drugs had come from. The integrity of the drug supply in Florida had reached this point because of lax state laws that literally allowed anyone to set up shop as a wholesaler or distributor. Florida subsequently changed its laws and is trying to regain control over the drug supply. What is distressing about this story is that while Florida recognized it needed stronger regulation of drug distribution, the U.S. Congress seems to want to move in another direction for the country as a whole.

In their so-called "blitz" operations looking at prescription products entering the U.S. through Customs-overseen mail facilities, FDA and U.S. Customs and Border Protection officials discovered many alarming things about the products American patients were receiving after they had ordered what they thought were appropriate substitutes for the prescriptions they generally filled at their local pharmacies. We think many of those patients believed they were going to get an FDA-approved product, from a country very similar to the U.S. in the strength of its regulatory system. But what they actually were sent often was not even close. Many of the products patients thought they would receive from Canada had their origins in some of the countries of the world where more than half of the drug supply is fake. Some of the products were packaged in sandwich bags; some were labeled in a foreign language; and some tablets or pills were smashed. What particularly concerned BIO was the presence in some of those shipments of biological products that should not be directly available to patients because they need to be administered by a health care provider or their administration needs to be overseen by a

provider. Further, some products that should remain refrigerated up to the point of their use were shipped by ordinary mail, with no refrigerant. We think those facts support our contention that even under the current system, patients are exposed to risk and that any system that would loosen controls, even one that tries to exempt certain particularly sensitive products, would almost certainly increase those risks.

Recently, U.S. Customs officials stated that every day about 40,000 parcels containing prescription drugs come into the New York City mail facility. Thousands more enter the country via the other 10+ mail facilities, including Miami and Chicago. Both Customs and the FDA have stated repeatedly that resource constraints alone prevent them from controlling and policing this overwhelming quantity.

Loosening controls on the importation of non-U.S.-approved prescription drugs would be a dramatic change not only in policy but also in the signals America sends to those who would enter the U.S. pharmaceutical market without following today's rules. Experience has shown, and continues to show, that unscrupulous and dishonest actors can, even under the most stringent of controls, become a part of the system. Today, they are discouraged from doing so because the message of our laws and regulations is that this is not permitted and that they could be penalized for breaking the law. Changing that message reverses the incentives and undermines the system.

Potential Impact on Biotechnology R&D

In the biotechnology industry, there is a plethora of ideas and a growing treasure trove of biological knowledge on which to build discovery. The reality, however, is that converting the knowledge and ideas into benefit for patients is time-consuming, costly, and high-risk. A marketplace that holds promise for appropriate return on that investment of time and resources is essential, especially for those biotechnology innovators who rely heavily on investment capital. Today, the U.S. is that marketplace. But that can change very quickly, as a result of a shift in health, economic, or trade policy, or for other reasons.

This leads to BIO's response to the specific question of the impact of importation proposals on research and development of new drugs. The answer, we believe, is not whether there will be such an impact, but the extent of the damage that would be done to the drug R&D enterprise and, in particular, to biotechnology R&D. To respond, we raise several hypothetical possibilities.

First, let us assume that the U.S. market is open to any purported prescription drug product – regardless of its worldwide regulatory status. In such a scenario – which is one in which counterfeiters thrive – the incentive for R&D would be considerably reduced and there would certainly be little or no reason to seek FDA approval for a new product. Investing in R&D would simply be unthinkable in light of a marketplace in which competitors could enter without any such expenditure.

A second scenario is one in which products could be legally imported if they have been approved by a regulatory authority in another country. The impact on R&D in such a scenario is perhaps more complicated, but clearly the incentives at least would be shifted, perhaps encouraging R&D to move outside the U.S. and almost certainly ensuring that U.S. patients would no longer be the first to realize the benefits of breakthrough biotechnology products, as companies would be seeking marketing approval in other countries first. The impact of this approach on the viability and desirability of the FDA approval system seems clear, however. Today, an FDA approval is a gold star. But often, securing FDA approval is more difficult and may take substantially longer for biotechnology products than obtaining approval in another country. Today, the reason for gaining FDA approval is to gain entry into the U.S. market. If products not approved by FDA can enter the U.S. market legally, there would be an extremely strong incentive to seek approval where it can be obtained more easily; the FDA approval system quickly could become an anachronism. The adverse consequence of this falls more heavily on patients than on product sponsors. The FDA approval has been patients' life insurance – their prescription products meet the gold standard.

A final scenario we raise is one in which importation is legalized only for products that are FDA approved, but are manufactured, warehoused, or for other reasons are in facilities outside the U.S. Today, such importation is legal only if the importer is the manufacturer of the product. We have serious concerns about the safety implications of changing that requirement, and also about the impact on investment in biotechnology R&D.

Again, we note that biotechnology investment is very sensitive to changes in health policy (among many other factors), and even changes in health policy that never come to pass can affect the investment picture. For example, when broad health care reform was proposed in the early 90's, investment dropped dramatically, not because policy had changed but because those who make investment decisions are zealously cautious in the face of uncertainty. Similar effects have been seen when Medicare reimbursement changes have been proposed and when changes in FDA approval standards have been discussed. Uncertainty about the value of U.S.-based R&D and U.S.-developed and -produced products, and about potential competition from sources heretofore not permitted in the U.S. market will affect investment, perhaps unpredictably but certainly.

The U.S. pharmaceutical marketplace is undoubtedly the most attractive in the world. That is certainly the reason it is attractive to counterfeiters and other criminals whose goal is making money, without regard to public health or safety. But the attractiveness of the U.S. market is also among the reasons that biotechnology innovation thrives here and that American patients often are the first in the world to have access to and benefit from innovative medicines. In summary, meddling in the consumer marketplace has implications – almost never in the best interest of consumers.

Safety Questions

Turning now to the question of how or if safety could be ensured if current restrictions on importing prescription products were loosened: in short, BIO believes that snipping the threads of the drug distribution safety net will invite further corruption and dishonesty. The U.S. regulatory system cannot stem today the shipment to American patients of thousands of unregulated prescription drug products. The Commissioner of Food and Drugs and other senior agency officials, as well as officials of U.S. Customs and Border Protection, have told Congress and the public multiple times that the agencies do not have the capacity to deal with the current influx of products. Would it be possible, with drug products entering the U.S. from multiple outside sources over which FDA may have little or no regulatory control, for FDA to ensure safety? History seems to suggest not.

In the late 1980's, Congress amended the Food, Drug, and Cosmetic Act, among other things, to close a statutory loophole through which prescription drug products were being imported into the U.S. under the guise that they were "American goods returned" or "re-imported" drugs. A drug diversion submarket developed that prevented effective control over the true sources of drugs. Unapproved, contaminated, subpotent, expired, and phony products entered the country under this pretext, and those bringing them in promised consumers the products were "the same as the one you always get in your drugstore." Consumers were harmed, and Congress responded by overwhelmingly supporting legislation to stop this risky and misleading practice through provisions of the Prescription Drug Marketing Act that required such "re-importation" to be done only by the original manufacturer. That requirement has meant that FDA-approved products are brought into the U.S. under proper storage and handling conditions, with an appropriate paper trail to assure their pedigree, and by an entity over which the FDA has unambiguous regulatory control. Modification of this system begs for a return to the pre-PDMA days and invites into our drug distribution system those with whom there is no clear and absolute FDA regulatory nexus. This can only mean risk for consumers.

Some would argue that this consumer risk can be reduced or even eliminated by providing FDA with new authority, including authority to test products, require certifications and other paperwork guarantees, require manufacturers and shippers to employ anti-tampering and anti-counterfeiting technology, and institute other mandates if needed. BIO wants to remind the Task Force, as FDA reminds our companies frequently, that quality, purity, and potency cannot be tested into products. End-product and end-process testing cannot substitute for a comprehensive, systematic, and constant vigilance in manufacturing, handling, and shipping. Such testing, moreover, cannot detect everything that may be potentially risky about a product. In many cases, especially with highly sensitive biological and biotechnology products, the only way to ensure safety and effectiveness is to know precisely what has happened at every step of the way, from manufacturing facility to purchaser. Analytical testing at the last stage simply cannot substitute for this. Moreover, any regimen of testing that would be credible could be extremely expensive, thus adding cost that presumably would be passed along to consumers, raising the further question of whether and to what extent such an importation scheme would result in lower prescription drug costs.

Some suggest, in addition to testing, that there be required certifications by importers regarding the sources of the products, routes and conditions of their travel, etc. While responsible wholesalers, distributors, and pharmacists can be expected to make honest certifications, pre-PDMA experience, as well as today's experience with proliferating dishonest sources of so-called "just the same as" drugs, shows that many who want to bring products into the U.S. are quite willing to fabricate documents and to claim things about the products that are, quite simply, false. BIO believes that it is extremely risky to hinge consumer safety on the unsupported belief that even the most stringent paperwork requirements will not be subverted by those with dishonest or malevolent intent.

FDA and Customs and Border Protection officials have said many times that they will require substantial additional resources to "regulate" a much-loosened import system. If we accept that there could be regulatory or legislative changes regarding imports that could ensure a "safe" system – which BIO does not concede – any such changes would necessarily have to be accompanied by significant and continuing additional appropriations for FDA. In his recent testimony before the Senate Commerce Committee, then-FDA Commissioner McClellan reminded the Senators that Congress provided on the order of $100 million to FDA for additional staff and related resources to regulate imported foods. This amount of additional funds, he said, would be insufficient to ensure the safety of tens of thousands of shipments of prescription drugs into the U.S.

The ingenuity and skill of counterfeiters and others who are undermining the drug distribution system today cannot be underestimated. They have shown that they can copy product color, shape, and company-proprietary marking; packages and labels; and, in short, literally everything about products so effectively that it is virtually impossible to detect what is authentic and what is not. Criminals have demonstrated the ability to replace clear liquid biological products with diluted ingredients or with plain water, without any visible evidence of tampering with vials. Authentic product vials have been stolen from the waste cans of health care providers, refilled with ineffective liquids, and resealed. Companies' proprietary labeling has been purchased from printing houses and used on packages that contained something completely unrelated to the actual product. Drug products have been imported, under the "import for export" provisions of the law; the bottles have been emptied and refilled with similar-looking vitamin tablets, then "re-exported," as required by law; and the now-opened, re-packaged and probably contaminated drug products have been sold on the U.S. black market. These are people with a very high financial incentive to be in the U.S. prescription drug market and a very low regard for consumer safety. Those financial incentives have not diminished and there is no reason to believe that these same people will shrink from their endeavors when all they need to do is falsify some paperwork to get their products on this market.

Anti-counterfeiting Technology Not a Panacea

Furthermore, the use of anti-counterfeiting technology, while it may be helpful in some areas, is not "the answer" to this issue. First, the incorporation of such technology will not be without its own difficulties. It may be especially challenging to incorporate the

technology in biological products, which tend to be formulated and packaged much differently from conventional pills and tablets. Some technologies, to work as desired and to thwart facile copying, must be incorporated into the product itself. There will be critical questions about whether and to what extent this might interfere with the effectiveness or safety of the product. There also will be the need to work with FDA to ensure that the regulatory requirements related to the use of such technology do not impede the timely approval and availability of new products. BIO agrees with the earlier conclusion of the FDA Counterfeiting Task Force, that while anti-counterfeit technology may be helpful as part of an approach to protecting the integrity of the drug supply, it should not be viewed as the answer and certainly cannot be used as a rationale or an excuse for loosening import regulation.

Conclusion

The challenges associated with protecting the safety and effectiveness of biological and biotechnology products are different from and in many cases greater than those associated with conventional drug products. Any system that loosens regulation increases these challenges to the point where it is essential to have different rules in place for these two categories of medicines. Congress has recognized this necessity by exempting biological and biotechnology products from its importation proposals – an exemption that we believe is necessary but not sufficient to ensure safety for patients. Exemptions are like delicate fabric – workable as long as they don't develop snags and holes. We simply do not believe that a lower regulatory standard than exists today for imported drug products is workable, whether the system exempts especially sensitive products or not.

Finally, there is the yet-unanswered question of whether, indeed, consumers would realize significant savings. With a new set of regulatory requirements, perhaps including certification of importers and significant analytical testing of products, there will be additional costs in the system. An appropriately regulated importation system is not the same as personal travel by individual consumers to a Canadian pharmacy of their choice. A well-regulated system involves third parties who will need to meet sufficient requirements to continue to ensure product safety. This will not be without cost – cost that will, in the end, be borne by consumers.

By virtue of its charge, it seems this Task Force is not being asked to change the current situation by reducing the number of illegal actions but, instead, to reduce the influx of illegal products by legalizing them. This is the ultimate Hobson's choice: Option one is to acknowledge that U.S. consumers do not need the imprimatur of an FDA approval as assurance that their prescription medications are safe and effective and that paperwork certifications and occasional testing can replace the certainty of FDA-regulated manufacturers moving their own products from one country to another. The alternative, option two, is to affirm, as two HHS Secretaries already have done, that loosening import controls will result in a reduction of safety and may, in the end, not result in cost-savings for consumers. BIO strongly urges the latter course.